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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/672,280	09/26/2003	Gregory Alan Lazar	067461-5121US	8317

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EXAMINER
CROWDER, CHUN

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/672,280	LAZAR ET AL.	
	Examiner	Art Unit	
	Chun Crowder	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02/13/2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-38,40-51,53-55,57-59,61-63,65 and 67-87* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 6, 7, 10-14, 16, 18, 19, 21-28, 34, 40, 41, 59, 63, 79, 80, 86, and 87* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/27/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 5,8,9,15,17,20,29-33,35-38,42-51,53-55,57,58,61,62,65, 67-78 and 81-85.

DETAILED ACTION

1. Applicant's amendments, filed on February 13, 2007, are acknowledged.

Claims 4, 39, 52, 56, 60, 64, and 66 have been previously canceled.

Claims 1-3, 5-38, 40-51, 53-55, 57-59, 61-63, 65, 67-87 are pending.

Claims 5, 8, 9, 15, 17, 20, 29-33, 35-38, 42-51, 53-55, 57, 58, 61, 62, 65, 67-78, and 81-85 have been withdrawn from further consideration under 37 C.F.R. 1.142(b) as being drawn to nonelected inventions.

Claims **1-3, 6, 7, 10-14, 16, 18, 19, 21-28, 34, 40, 41, 59, 63, 79, 80, 86, and 87** are under consideration in the instant application as they ready on the originally elected invention of Group I and species an antibody, IgG1, targeting CD20, 239D substitution, increased affinity for FcγR and no carbohydrate modification.

2. This Office Action will be in response to applicant's arguments, filed on February 13, 2007.

The rejections of record can be found in the previous Office Actions, mailed on July 26, 2006 and November 16, 2006.

3. Applicant's argument regarding the support of position 332 in the priority document USSN 60/414,433 is acknowledged. Applicant argues that the support for amino acid substitution at position 239 of the Fc region can be found in Figure 2, 7 and 8 of the USSN 60/414,433.

However, it is noted USSN 60/414,433 only provide support for certain specific amino acid substitutions in position 239 of the Fc region (e.g. substitutions with amino acids E or R) (e.g. see Figure 2) and USSN 60/414,433 does not provide support for 239D substitution; such disclosure of species in the priority document cannot support the instant claims encompassing a genus of amino acid substitutions at position 239 of the Fc region.

The instant claims now recite limitation of position 239 and/or 239D of the Fc region which were not clearly disclosed in the priority application and would have changed the scope of the priority application.

Further, the priority application has not provides a sufficient description of a representative number of species to represent the entire genus of amino acid modification in position 239 of the Fc region as currently claimed.

It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

Therefore, reliance upon the species of disclosure of 239 (e.g. substitutions with amino acids E or R) in the priority document does not provide sufficient written description for amino acid modification in position 239 of the Fc region as currently claimed.

Further, given that applicant has not provided showing that specifically supports the instant claimed limitation of amino acid substitution at position 239 in the Fc region in priority documents USSN 60/442,301, the instant claims have not been accorded the priority of these two priority documents.

4. In light of applicant's amendment to the claims, the prior rejections under 35 U.S.C. 112, second paragraph and first paragraph, enablement and written description have been withdrawn.

5. In view of the cancellation of the limitation of "position 239" in the copending USSN 10/822,231, the previous nonstatutory obviousness-type double patenting rejection over USSN 10/822,231 has been withdrawn.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1-3, 6, 7, 10-14, 16, 18, 19, 21-28, 34, 40, 41, 59, 63, 79, 80, 86, and 87 are rejected under **35 U.S.C. 102(b)** as being anticipated by Presta (WO 00/42072. Reference B1 on IDS) for reasons of record set forth in the previous Office Actions mailed on July 26, 2006 and November 16, 2006.

Applicant's arguments have been fully considered but have not been found persuasive.

Applicant argues the followings:

A) Applicant argues that Presta does not teach the instant antibody or immunoadhesin comprising an Fc variant encompassing at least one amino acid substitution at position 239 wherein said Fc variant increases binding affinity to an Fcγ receptor (FcγR) as compared to the parent antibody or immunoadhesin.

Applicant argues that Presta does not teach the claimed species of position 239 in the Fc region and the claimed functional limitation of increased binding to an Fcγ receptor. Applicant focuses the Presta's teachings on the working example shown in Table 6 in that S239A displays reduced binding to FcγRIII and FcγRII (see page 71, in particular). Applicant further argues that Presta does not teach any specific substitution at position 239 that has the claimed functional limitation of increased binding affinity to an FcγR. Furthermore, applicant argues that Presta teaches a genus of making modifications at numerous positions in the Fc region; such genus would not anticipate the claimed species of the claimed amino acid substation at position 239 of the Fc region with increased binding affinity to an FcγR.

This is not found persuasive for following reasons:

In contrast to applicant's assertions based upon the working examples of Presta, it is noted that a prior art reference must be considered in its entirety. See MPEP 2141.02.

In this case, Presta clearly identifies that position 239 of the Fc region of the parent polypeptide can be substituted with any other amino acid residues including aspartic acid (D) other than the parent residue serine (S) (e.g. see pages 14-15). Presta further teach that the preferred substitution for Serine (S) is Threonine (T) (see Table 1 on page 24, in particular). Therefore, the teachings of Presta are not limit to S239A as applicant asserts.

Further, contrary to applicant's assertion that Presta teaches a genus of positions with amino acid substitutions, it is noted that when the species is clearly named, the species claim is anticipated no matter how many other species are additionally named. Ex parte A, 17 USPQ2d 1716 (Bd. Pat. App. & Inter.1990). Also see MPEP 2131.02.

Here, even if Presta discloses a genus of natural and non-natural amino acids and various positions in the Fc region, Presta clearly teaches that the position 239 of the Fc regions can be substituted with amino acid residues including aspartic acid (D) and Threonine (see Table 1 on page 24, in particular); as such, Presta clearly names the claimed species.

The comprehensiveness of the explicit listing of the known naturally occurring amino acids and disclosed non-naturally occurring amino acids in Presta does not negate the fact that the amino acid substitutions by aspartic acid (D) or Threonine (T) in position 239 of the Fc region as claimed are specifically taught.

Furthermore, regarding the claimed functional limitation of increased binding to an FcγR for the Fc variant with amino acid substitution in positon 239, it is noted that when the claimed product and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

In this case, given the reference antibody variant comprises amino acid substitution at the same position (239) with the same residue aspartic acid (D) as the claimed polypeptide variant comprising an Fc variant, the claimed functional limitations associated with the polypeptide variant would be inherent properties of the referenced polypeptide.

In conclusion, applicant's arguments have not been found persuasive.

B) Applicant asserts that Presta's teaching of position 239 and the separate teaching of amino acid substitutions do not anticipate the elected species of 239D.

Applicant's arguments in conjunction with various legal citations have been fully considered but have not been found persuasive.

Applicant argues that Presta does not separately and clearly name a 239D Fc variant. Further, applicant argues that one skilled in the art would not know that position 239 can be chosen for the function of increased binding to an FcγR. Furthermore, applicant asserts that Presta leads one of ordinary skill in the art away from variants at position 239 for increased binding to an FcγR.

This is not found persuasive for reasons stated above in Section (A), as well as followings:

Contrary to applicant's assertion, it is noted once again, that a prior art reference must be considered in its entirety. See MPEP 2141.02.

In this case, in contrast to applicant's assertion that Presta does not separately and clearly name a 239D Fc variant, it is noted that the amino acids substations including all natural occurring residues taught by Presta (e.g. see pages 14-15 and Table 1 on page 24) must be read in the context of the entire teachings of the reference, which are directed to amino acid substitutions in the Fc region including position 239. Thus, Presta clearly teaches the claimed antibody or immunoadhesin comprising an Fc variant comprising amino acid substitutions with residues including D or T at position 239.

Further, contrary to applicant's assertion that one skilled in the art would not know that position 239 can be chosen for the function of increased binding to an FcγR, it is noted that Presta identifies that position 239 in the Fc can be chosen for altering binding affinity with an FcγR (e.g. see pages 5-8) when residue S239 is substituted with any other naturally occurring amino acid residues including D or T, one skill in the art would recognizes that such substitutions would lead to the function of increased binding to an FcγR. Since applicant's own specification discloses that it is known in the art that mutagenesis experiments are often carried out to determine the rold of certain residues in protein structure and functions (see page 55-56 of the instant specification), one of skill in the art would know position 239 can be chosen for the function of increased binding to an FcγR.

Furthermore, regarding applicant's assertion that the reference leads one of ordinary skill in the art away from variants at position 239 for increased binding to an FcγR, it is noted that A reference is no less anticipatory if, after disclosing the invention, the reference then disparages it. The question whether a reference "teaches away" from the invention is inapplicable to an anticipation analysis. Celeritas Technologies Ltd. v. Rockwell International Corp., 150 F.3d 1354, 1361, 47 USPQ2d 1516, 1522-23 (Fed. Cir.1998).

Here, given that Presta teach the same antibody or immunoadhesin comprising a variant Fc comprising amino acid substitutions in the same position with the same amino acid residues as currently claimed, the teachings of Presta is anticipatory to the claimed invention and applicant's arguments that Presta leads one of ordinary skill in the art away for the variants at position 239 is has no bearings to anticipation analysis.

Moreover, it is noted that reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. "Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention." In re Donohue, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985).

In this case, Presta clearly teach that the amino acid residue S in position 239 in the Fc region can be substituted to any other naturally occurring amino acid residues including D or T for altered binding to an FcγR. One of ordinary skill in the art could have combined the teachings of Presta with his or her own knowledge to make the claimed antibody or immunoadhesin comprising an Fc variant comprising 239D.

In addition, applicant asserts that the Examiner cited *In re Sivaramakrishnan* (see page 19 of the Remark). It is not clear when and where *In re Sivaramakrishnan* was cited by the Examiner.

In conclusion, applicant's arguments have not been found persuasive. The reference teachings anticipate the claimed invention.

8. Claims 1-3, 6, 7, 10-14, 16, 18, 19, 21-28, 34, 40, 41, 59, 63, 79, 80, 86, and 87 are rejected under 35 U.S.C. 102(e) as being anticipated by Presta (US Patent 6,737,056. Reference A97 on IDS) for reasons of record.

Applicant's arguments have been fully considered but have not been found persuasive.

Applicant's arguments and the Examiner's rebuttal regarding the teachings of Presta are essentially the same as discussed above in Section 8.

Further, Presta (US Patent 6,737,056) not only teaches but also claims a variant of a parent polypeptide comprising a human IgG1 Fc region that comprising an amino acid modification at positions including 239, wherein said variant has increased binding to an FcγR (e.g. see claims 13 and 14).

Therefore, the reference teachings anticipate the claimed invention.

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Given the absence of additional rebuttal in applicant's amendment to the outstanding nonstatutory obviousness-type double patenting rejections of record over USSNs: 11/483,378, 11/483,250, 11/124,620, and 11/396,495, the rejections are maintained for reasons of record.

11. Since applicant was aware or should have been aware of the copending applications listed below; the provisional double patenting rejection is made for reasons of record and discussion below, and the Office Action is made FINAL.

12. Claims **1-3, 6, 7, 10-14, 16, 18, 19, 21-28, 34, 40, 41, 59, 63, 79, 80, 86, and 87** are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over:

Claim 1 of copending USSN:11/495,242,
Claims 1, 4-17, 20-24 of copending USSN: 11/544,165,
Claims 1-17, 21-31, 33-35, 38 and 40-42 of copending USSN: 11/618,457,
Claims 1-17, 21-31, 33-35, 38, and 40-42 of copending USSN:11/618,472,
Claims 1-17, 21-31, 33-35, 38, and 40-42 of copending USSN:11/618,488,
Claims 1, 3, 5, 6, 9, and 11-13 of the copending 11/764,001,
Claims 1, 3, 5, 6, 9, and 11-13 of the copending USSN: 11/765,353,
Claims 1, 3, 5, 6, 9, and 11-13 of the copending USSN: 11/765,390,
Claims 1, 3, 5, 6, 9, and 11-13 of the copending USSN: 11/765,402, and
Claims 1, 3, 5, 6, 9, and 11-13 of the copending USSN: 11/766,609.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant and the copending application claims are drawn to same or nearly the same polypeptide variants with the same modifications to the Fc region at position 239 for altered affinity for FcγRs and effector functions. Given polypeptide variants rely on the same amino acid modification, the instant claims and the conflicting claims would anticipate or render obvious of one another.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

13. Claims **1-3, 6, 7, 10-14, 16, 18, 19, 21-28, 34, 40, 41, 59, 63, 79, 80, 86, and 87** are directed to an invention not patentably distinct from

Claims 38-43 45 and 46 of commonly assigned USSN 11/483,378,
Claims 1-12 of commonly assigned USSN 11/124,620,
Claims 1-19 of commonly assigned USSN 11/396,495,
Claim 1 of commonly assigned USSN:11/495,242,
Claims 1, 4-17, 20-24 of commonly assigned USSN: 11/544,165,
Claims 1-17, 21-31, 33-35, 38 and 40-42 of commonly assigned USSN: 11/618,457,
Claims 1-17, 21-31, 33-35, 38, and 40-42 of commonly assigned USSN:11/618,472,
Claims 1-17, 21-31, 33-35, 38, and 40-42 of commonly assigned USSN:11/618,488,
Claims 1, 3, 5, 6, 9, and 11-13 of commonly assigned 11/764,001,
Claims 1, 3, 5, 6, 9, and 11-13 of commonly assigned USSN: 11/765,353,
Claims 1, 3, 5, 6, 9, and 11-13 of commonly assigned USSN: 11/765,390,
Claims 1, 3, 5, 6, 9, and 11-13 of commonly assigned USSN: 11/765,402, and
Claims 1, 3, 5, 6, 9, and 11-13 of commonly assigned USSN: 11/766,609.

for reasons stated above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned USSNs: 11/483,378, 11/396,495, 11/124,620, 11/495,242, 11/544,165, 11/618,457, 11/618,472, 11/618,488, 11/764,001, 11/765,353, 11/765,390, 11/765,402, and 11/766,609 discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Crowder whose telephone number is (571) 272-8142. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chun Crowder, Ph.D.
Patent Examiner
August 7, 2007

MAHER M. HADDAD
PRIMARY EXAMINER